REMARKS

Claims 1 and 2 are pending in the instant application. Claims 1 and 2 have been rejected. Claims 1 and 2 have been amended. Support for these amendments is provided in the specification at page 4, lines 9 through 19. Thus, no new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 1 and 2 under 35 U.S.C. § 102(a)

Claims 1-2 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Schmaier. The Examiner suggests that Schmaier (U.S. Patent 6,544,750) teaches PAR-1 as a specific substrate of thrombin and its expression by platelets.

At the outset, Applicants respectfully disagree with the Examiner's characterization of this reference as a 102(a) reference. This patent published on April 28, 2003, well after the December 21, 2000 priority date of the instant application. Thus, the patent is not a reference by another published prior to the filing date of the instant application. Since the filing date of this patent precedes the filing date of the instant application, Applicants will address this rejection as if raised

under 35 U.S.C. § 102(e).

Applicants respectfully disagree with the Examiner's suggestion that the teachings of Schmaier et al., which relate only to PAR-1 mediation of platelet aggregation, thrombosis and cell activation, and provide no teaching whatsoever with respect to PAR-4 or GP Ib, anticipate the instant invention. This reference also provides no teaching whatsoever with respect to inhibition of the β-thrombin and γ-thrombin pathways.

As made clear in the teachings of the instant specification, the present invention relates to the discovery of distinct thrombin-induced platelet activation pathways for α-thrombin, β-thrombin and γ-thrombin, as well as receptor PAR-1, PAR-4 and GP Ib and the ability to identify and/or develop new anti-thrombotic/anti-platelet therapies based upon selective modulation of these pathways and interactions with GP Ib and PAR-4 as well as PAR-1. The instant patent application sets forth for the first time that α-thrombin selectively activates GP Ib and that β-thrombin and α-thrombin activate selectively PAR-4. See, for example, teachings at page 4, lines 9-19, and page 6, lines 2-22 of the specification. As taught therein, it is the ability to co-activate these newly discovered distinct pathways

which results in a synergistic effect on thrombin-induced platelet activation.

In an earnest effort to advance the prosecution of this case and to clarify distinctions of the present invention over prior art references such as Schmaier et al., Applicants have amended the claims to state that activity against all three receptors, namely GP Ib, PAR-4 and PAR-1, or all three thrombin pathways, namely the α-thrombin, β-thrombin, and γ-thrombin pathways, are monitored and that activity as an inhibitor of GP Ib and PAR-1 or PAR-4 binding is indicative of anti-thrombotic/anti-platelet activity of the compound.

Since Schmaier et al. provides no teaching whatsoever with respect to PAR-4 or GP Ib receptors or β-thrombin and γ-thrombin pathways this reference cannot anticipate the claims as amended.

Withdrawal of this rejection under 35 U.S.C. § 102(a) or (102(e) is therefore respectfully requested.

II. Rejection of Claim 1 under 35 U.S.C. § 102(b)

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by each of Coughlin, Hollenberg and South.

The Examiner suggests that Coughlin (WO 99/43809) teaches

screening candidate compounds for their ability to act as agonists or antagonists to the effects of interaction between thrombin and PAR 4.

The Examiner suggests that Hollenberg teach agonist assays for PAR-1 and 2 using a platelet aggregation assay.

The Examiner suggests that South teaches inhibitors of the von Willebrand Factor platelet glycoprotein 1b interaction.

Thus, the Examiner suggests that all the claimed features are taught by the above references for the same function as claimed.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that the teachings of South relating to inhibitors of the von Willebrand Factor platelet glycoprotein 1b interaction relate to the same function as claimed. Claims of the instant application are specifically drawn to monitoring activity of a compound to inhibit **thrombin-induced** platelet aggregation. This interaction is thus different from interactions with von Willebrand Factor as taught by South.

Further, as discussed in Section I, *supra*, the claims of the instant application have been amended and are now drawn to screening methods wherein activity of a compound against all

three receptors, namely GP Ib, PAR-4 and PAR-1, or all three thrombin pathways, namely the α-thrombin, β-thrombin, and γ-thrombin pathways, are monitored. None of the prior art references teach a method wherein more than one receptor or pathway is monitored. Further, none of the references teach a method wherein β-thrombin or γ-thrombin pathways are monitored.

Thus, none of the cited references alone, or in combination teach or suggest all the elements of the claims as amended.

Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

III. Rejection of Claims 1-2 under 35 U.S.C. § 103(a)

Claims 1 and 2 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Xu. The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the method of Xu to screen for drugs to inhibit GP Ib, PAR-1 or PAR-4 binding in a platelet aggregation assay because Xu teaches peptide fragments which are derived from platelets and have the same function as the platelet receptor. The Examiner suggests that the function of the derived fragments and platelets in the assays taught by Xu

would be expected to be the same.

Applicants respectfully traverse this rejection.

Teachings of Xu et al. relate to PAR-4 polynucleotides and polypeptides. There is also brief mention of PAR-1 in the background section. Nowhere, does this reference mention GP Ib. Nowhere does this reference mention β-thrombin and γ-thrombin pathways. Further, this reference neither teaches nor suggests a method as now claimed for screening activity of a compound against all three receptors, namely GP Ib, PAR-4 and PAR-1, or all three thrombin pathways, namely the α-thrombin, β-thrombin, and γ-thrombin pathways.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP§2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations.

Xu et al., which is silent with respect to the GP Ib receptor and the β-thrombin and γ-thrombin pathways clearly fails

to meet any of these criteria with respect to claims drawn to a method wherein activity against the GP IB receptor or β-thrombin or γ-thrombin pathways is screened.

Withdrawal of this rejection under 35 U.S.C. § 103(a) is therefore respectfully requested.

IV. Rejection of Claims 1-2 under 35 U.S.C. § 112, first paragraph

Claims 1-2 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner suggests that the claims are directed to screening for compounds but the specification shows no compounds that have the activities as claimed.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that compounds with the ability of inhibit one or more of the receptors are not shown in the instant specification. Multiple compounds with the ability to inhibit GP Ib, PAR-1 and/or PAR-4 are disclosed throughout the specification. See, for example, page 5, lines 6 through 13 wherein the chemically defined PAR-1 inhibitor SCH203099 and

anti-PAR-1 antibody are described. Also see page 5, line 28 wherein LJ Ib-10, an anti-GP Ib antibody is described.

Further, MPEP § 2164 is clear; the invention that one skilled in the art must be enabled to make and use is that defined by the claims of the particular application or patent. In the instant application the claims are drawn to methods for screening for compounds having anti-thrombotic/anti-platelet activity. Thus, it is a screening method and not "compounds that have the activities as claimed" as suggested by the Examiner which must be enabled.

The test of enablement, as set forth in MPEP § 2164.01 is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. Detailed methodologies for monitoring inhibition of thrombin binding to respective receptors and/or an inhibitor binding selectively to different thrombins via platelet aggregation assays are taught in the specification at page 4, line 26, through page 10, line 26. Thus, the instant specification clearly teaches one of skill in the art how to screen a compound for activity to inhibit thrombin-induced platelet aggregation through inhibition of GP Ib, PAR-1 and PAR-4 receptor binding or

inhibition of α-thrombin, β-thrombin, and γ-thrombin pathways as claimed. Accordingly, the instant specification meets the enablement requirements of 35 U.S.C. § 112, first paragraph, for the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph is therefore respectfully requested.

V. Rejection of Claims 1-2 under 35 U.S.C. § 112, second paragraph

Claims 1-2 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner suggests that "platelet activity of what" is not recited, that recitation of "the ability" of a compound is improper because compounds have activities and that "the compound" in the last line of claim 1 lacks antecedent basis.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the claims to recite that the activity is of the compound being tested, to replace the term

"ability" with --activity-- and to state --said compound-- as opposed to "the compound" in accordance with antecedent basis provided in line 1 of step b) of claim 1.

Withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is therefore respectfully requested.

VI. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable 13econsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **August 3, 2004**

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